

60th Medical Group (AMC), Travis AFB, CA

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY

(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20150014A

DATE: 8 January 2016

PROTOCOL TITLE: "Partial Resuscitative Endovascular Balloon Occlusion of the Aorta (P-REBOA) in a pig model (*Sus scrofa*) with ongoing resuscitation."

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Maj Lucas Neff

DEPARTMENT: General Surgery

PHONE #: 423-5179

INITIAL APPROVAL DATE: 19 February 2015

LAST TRIENNIAL REVISION DATE: N/A

FUNDING SOURCE: SG

1. RECORD OF ANIMAL USAGE:

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
<i>Sus Scrofa</i>	68	0	17

2. PROTOCOL TYPE / CHARACTERISTICS: (Check all applicable terms in EACH column)

Training: Live Animal Medical Readiness Prolonged Restraint
 Training: non-Live Animal Health Promotion Multiple Survival Surgery
 Research: Survival (chronic) Prevention Behavioral Study
 Research: non-Survival (acute) Utilization Mgt. Adjuvant Use
 Other () Other (Treatment) Biohazard

3. PROTOCOL PAIN CATEGORY (USDA): (Check applicable) C D E

4. PROTOCOL STATUS:

*Request Protocol Closure:

Inactive, protocol never initiated
 Inactive, protocol initiated but has not/will not be completed
 Completed, all approved procedures/animal uses have been completed

5. Previous Amendments:

List all amendments made to the protocol.. IF none occurred, state NONE. Do not use N/A.

For the Entire Study Chronologically

Amendment Number	Date of Approval	Summary of the Change
1	19 Mar 15	Biosamples
2	16 Apr 15	Personnel
3	16 Apr 15	Procedures

4	15 May 15	Personnel
5	15 May 15	Personnel
6	16 July 15	Biosamples

6. **FUNDING STATUS:** Funding allocated: \$59,920.00 Funds remaining: \$ 0.00

7. **PROTOCOL PERSONNEL CHANGES:**

Have there been any personnel/staffing changes (PI/CI/AI/TC/Instructor) since the last IACUC approval of protocol, or annual review? Yes No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

Capt Anders Davidson (AI) Yes, Dr. Sarah Ashley Ferencz (AI) Yes, Dr. Michael Johnson (AI) Yes

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

None.

8. **PROBLEMS / ADVERSE EVENTS:** Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

None.

9. **REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:**

REPLACEMENT (ALTERNATIVES): Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

No.

REFINEMENT: Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

No.

REDUCTION: Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

No.

10. **PUBLICATIONS / PRESENTATIONS:** (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).

11. **Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?**

Yes. The device described here has the potential to significantly improve the treatment of battlefield casualties.

12. **PROTOCOL OUTCOME SUMMARY:** (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

INTRODUCTION: Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) has emerged for treatment of non-compressible torso hemorrhage, but its efficacy is limited by the short duration of tolerable ischemia and resulting reperfusion injury. Endovascular Variable Aortic Control (EVAC) is a conceptual therapy that relies on regional permissive hypoperfusion to limit exsanguination while providing limited perfusion to distal tissue beds.

METHODS: In the absence of an endovascular device capable of EVAC, an automated extracorporeal circuit was developed to perform proof of concept testing of EVAC as an alternate resuscitative strategy. The circuit then underwent benchtop validation before being used in a large animal model of highly lethal uncontrolled hemorrhage.

A predetermined computer algorithm guides the regulation of aortic flow through the circuit based on the proximal hemodynamics of the exsanguinating animal.

RESULTS: Benchtop validation revealed tight control of flow through the circuit through all phases of the proposed study algorithm. Nine animals were used for animal development, with 7 animals surviving the initial surgical preparatory phase. Severe injury was accomplished via a large reproducible liver laceration resulting in profound hypotension prior to complete aortic occlusion. After 20 minutes of complete occlusion, regulated flow through an extracorporeal circuit provided perfusion to capillary beds distal to the complete occlusion. 2 animals had ongoing hemorrhage and required re-occlusion of the aorta, while 5 animals tolerated sustained, escalating restoration of distal blood. Following 70 minutes of partial aortic occlusion, damage control surgery and whole blood resuscitation was performed and all animals were survived to 360 minutes. Animals that tolerated distal flow had decreased levels of lactate, preserved renal function, and were weaned from aortic occlusion more rapidly.

CONCLUSIONS: Endovascular variable aortic control is capable of limiting exsanguination while providing blood flow to distal organs prior to definitive hemorrhage control. While there is no current endovascular device that possesses the ability to achieve EVAC, we have developed a novel automated extracorporeal circuit to establish the proof of concept. EVAC may be a new avenue for prolonged non-operative intervention and extend survival in an otherwise rapidly fatal injury. Further work is necessary to determine if distal hypoperfusion with this approach will confer a physiologic benefit compared to REBOA.

(PI/TC Signature)

11 Jan 2015

(Date)

Attachments:

Attachment 1: Defense Technical Information Center (DTIC) Abstract Submission (**Mandatory**)

Attachment 1
Defense Technical Information Center (DTIC) Abstract Submission

INTRODUCTION: Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) is limited by the short duration of tolerable ischemia and resulting reperfusion injury. P-REBOA relies on regional permissive hypoperfusion to limit exsanguination while providing limited perfusion to distal tissue beds.

METHODS: An automated extracorporeal circuit was developed to perform P-REBOA. The circuit was used in a large animal model of highly lethal uncontrolled hemorrhage.

RESULTS: Nine animals were used for animal development, with 7 animals surviving the initial surgical preparatory phase. Severe injury was accomplished via liver laceration resulting in profound hypotension prior to complete aortic occlusion. After 20 minutes of complete occlusion, regulated flow provided perfusion to capillary beds. Following 70 minutes of partial aortic occlusion, damage control surgery and whole blood resuscitation was performed and all animals were survived to 360 minutes. Animals that tolerated distal flow had decreased levels of lactate, preserved renal function, and were weaned from aortic occlusion more rapidly.

CONCLUSIONS: P-REBOA is capable of limiting exsanguination while providing blood flow to distal organs prior to definitive hemorrhage control. There is no current endovascular device that possesses the ability to achieve P-REBOA.

Grant Number: _____

From: _____

****If you utilized an external grant, please provide Grant # and where the grant came from. Thank you.**